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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/578,693	05/26/00	YAMANOUCHI M	20-4710P

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EXAMINER	
COOK, L	
ART UNIT	**PAPER NUMBER**
1641	5

DATE MAILED: 04/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/578,693	YAMANOUCHI ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2000*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2000* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4*.
18) ☐ Interview Summary (PTO-413) Paper No(s). _____.
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Please note that the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all correspondence regarding this application should be directed to Group Art Unit **1641**. All communications should be directed to **Lisa V. Cook**, whose telephone number is **(703) 305-0808**.

2. Claims 1-15 are pending and currently under consideration.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). This application does not contain the required first sentence of the specification referencing priority document foreign application No. 9-323684 filed 11/26/97 in Japan and foreign application No. 87119150 filed 11/19/98 in Taiwan. Please add to the specification.

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 9-323684, filed on 11/26/97. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

5. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Application No. 87119150 on 11/19/98. It is noted, however, that applicant has not filed a certified copy of the Taiwan application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

6. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 has cited the references they have not been considered.

7. The information disclosure statements filed 12/18/00-Paper#4 has been considered as to the merits prior to first action.

Drawings

8. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(2) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(i), three sets of drawings or photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Specification

9. The abstract of the disclosure is objected to because there appears to be a typo on line 8 wherein it recites "diagnosis of prognosis of". It is not clear if applicant intended to recite "diagnosis or prognosis of". Correction is required. See MPEP § 608.01(b).

10. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. For example "Method for examining kidney diseases by detecting the fatty acid protein α_{2U}-globulin".

11. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

12. The disclosure is objected to because of the following informalities: A typo appears on page 25, line 17. Nucleotide is misspelled "necleotide". Appropriate correction is required.

13. The use of the trademarks has been noted in this application. (.i.e. Superdex -page 27, line 3 and Sephacryl-page 23, line 1). All trademarks in the disclosure should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claims 1-15, the use of "examining" is vague and indefinite because it is unclear as to what the method is to entail. The term is not defined in the specification or the claims. Thus, as recited the metes and bounds of the claim can not be meet. Is it applicants' intent to mean that the method will detect kidney disease or some other disease that may be related to kidney disease, therein allowing for the examination of kidney disease? It is suggested that the claims specifically recite that kidney disease will be detected.

B. Claims 2, 9, and 11 are vague and indefinite because it is unclear as to what the terms liver-type, muscle-type, and kidney –type are to encompass. The claim recites a reactive compositions that are characterized by these terms, however without clear definition as to what the terms comprise the limitations are not clearly defined. It is suggested that the claims simply recite liver, muscle, or kidney in order to obviate this rejection. Please explain.

C. Claim 13 is vague and indefinite in utilizing the acronym GMB. Although the term may have art recognized meaning, it is not clear if applicant intends to claim the prior art definitions. In order to clearly recite this limitation it is suggested that the term be defined in its first instance. The initial explanation will convey intended meaning of subsequent abbreviations in the claims. Please not that GMB is not found in the disclosure, is this a typo and should be GBM (see the disclosure – page 33, lines 10-21).

D. The term "substantially" in claim 9, is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

15. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below:

The claims are drawn to a method detecting kidney disease. The claims are drawn to the development of an fatty acid binding complex, but does not indicate how the complex will be formed or identified (i.e. label). Merely reciting a method is not considered to be a proper method step. A method, as recited in the preamble of claim 1, requires at least a contact step between reagents and sample, a detection step, and a correlation step. Please include the appropriate assay steps. Further, there are no claimed steps reciting the washing or removal of unbound materials. If no separation will be performed it is unclear how the complex will be identified from the reaction solution (unbound material).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The methods of claims 1 and 10 have insufficient steps. These critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). There is no claimed steps reciting the washing/removal of unbound material. A separation step that removes bound and unbound material from the detection complex involving a fatty acid binding protein complex is missing. If you do not have a separation step after step (c), the addition of the fatty acid will always provide a positive result regardless of the bound/unbound reagents that are complexed and thus could not be utilized to detect kidney disease. Please add the removal of unbound reagents to the claims or clearly indicate the specific method of detection that does not employ the removal of unbound material.

17. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for detecting the fatty acid binding protein - α_{2U}–globulin, it does not reasonably provide enablement for any and all methods detecting any and all fatty acid binding proteins for any and all kidney disease detection. The claims, as written, read on any fatty acid binding protein capable of detecting any Kidney disease. *(claims 1and 10).*

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claim to detect *any and all kidney diseases* employing *any and all* fatty acid binding proteins, wherein detection of any fatty acid protein expressed by the animal is indicative of kidney disease in the animal. The only protein taught in the disclosure is α_{2U}-globulin.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1, 2, 4-8, 10, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536).

Olson et al. disclose a comparative study evaluating α_{2U}-globulin protein concentrations in male rat and human (males aged 30-40 with no clinical signs of renal disease) urine samples. The disclosure teaches that α_{2U}-globulin protein is a fatty acid binding protein (FABP) synthesized in the liver and introduced into the urine from the kidney or kidney tissue. See page 4, lines 2-3, page 7, lines 10-15, and page 9, line 14. The urinary proteins were separated by chromatography and SDS-polyacrylamide gel electrophoresis. Immunoidentification was accomplished via western blotting with polyclonal rabbit anti-rat α_{2U}-globulin antibody (page 526, 2nd column, 2nd paragraph) and biotinylated anti-IgGand avidin-horseradish peroxidase complex with 4-chloro-1-naphthol (page 526, 2nd column, 3rd paragraph).

The fraction of α_{2U}-globulin protein in rat urine was 26% of the total urinary protein content and in humans the fraction was 4% of the total urinary protein content. High amounts of α_{2U}-globulin proteins were associated with hyaline droplet nephropathy (HDN). Page 525, 1st column, 2nd paragraph) This study suggested that humans were at no risk for the particular kidney disease - hydrocarbon-induced nephropathy.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Kimura et al. (Journal of Biological Chemistry, 3/25/91, Vol.266., No.9., pages 5963-5972).

See discussion of Olson et al. as set forth above.

Olson et al. differ from the instant invention in failing to teach that the FABP (α_{2U}–globulin) is found in the proximal tubule of the kidney and does not cross-react with a heart muscle-type fatty acid binding protein.

However, these characteristics of α_{2U}–globulin were already known in the prior art. Specifically Kimura et al. disclose that fatty acid-binding proteins found in the kidney could be distinguished according to their primary structure and histologic distribution. Two specific FABPs weighing 14 and 15.5 kDa were found in male rat kidney cytosol. The 14 kDa compound was identified as heart FABP and localized in the cytoplasm of the epithelia of the kidney distal tubules. The 15.5 kDa compound was identified as a proteolytically modified form of α_{2U}–globulin (alpha 2u-globulin) and localized in the endosomes or lysosomes of kidney proximal tubules.

Olson et al., and Kimura et al. are all analogous art because they are from the same field of endeavor, both inventions teach methods involving α_{2U}–globulin detection.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the antibody which would not cross-react with a muscle-type fatty acid binding protein as taught by Kimura et al., to detect the specific kidney FABP in the method of Olson et al. because such antibodies as taught by Kimura et al. are well known in the art.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such antibody assays, because Kimura et al. had already taught that the kidney contained two different types of fatty acid binding proteins, one designated the heart-FABP and the other designated the kidney-FABP. (page 5964, Results).

One having ordinary skill in the art would have been motivated to distinguish between the two types by employing an antibody that would not cross react with the other type (heart-FABP/kidney distal tubules) in order to receive an accurate, more precise measure of the concentration of the FABP of interest (in this case kidney-FABP/ kidney proximal tubules).

II. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) in view of Galaske et al. (Pflugers Archives European Journal of Physiology, 1978, 375,3, 269-277-ABSTRACT ONLY).

Please see previous discussions of Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536).

Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) differ from the instant invention in not teaching a detection system involving an anti-GMB-nephritis model.

Galaske et al. disclosed the glomerular filtration and tubular uptake of plasma proteins in the acute heterologus phase of an anti-GMB nephritis model. Injections of anti-glomerular-basement membrane serum (anti-GMB-serum) were evaluated in tubular reabsorption and tubular flow. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a anti-GMB nephritis model as taught by Galaske et al., to detect kidney diseases via proteins in the method of Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) because such anti-GBM nephritis models as taught by Galaske et al. are well known in the art.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing anti-GBM nephritis models, because Galaske et al. disclose that such models existed allowing for protein detection in plasma and urine.

III. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Toxicology and Applied Pharmacology, Vol.102, 1990, pages 524-536) in view of Zuk et al. (U.S.Patent #4,281,061).

The teachings of Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) are set forth above. Although the reference teaches reagents for examining kidney disease, the reference fail to teach the assay as a kit.

However, Zuk et al. (4,281,061) teach that "as a matter of convenience the reagents [of an immunoassay} can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest" (column 22, lines 63-66). It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the kidney disease detection assay as taught by Olson et al. (Toxicology and Applied Pharmacology, Vol.102., 1990, pages 524-536) and format them into a kit because Zuk et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre measured amounts which eliminates the variability that can occur when performing the assay.

20. For reasons aforementioned, no claims are allowed.

Remarks

21. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Nagasawa (Japanese Med. Res. Found. Publ. 1979, 7 (Glomerulonephritis), pages 39-51)- ABSTRACT ONLY teach that the binding distribution of Con A is similar anti-nephritogenic glycoprotein antibody.

22. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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3/30/01

LONG V. LE
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